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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,531	03/23/2001	Bernhard Dietzschold	DIE01-NP001	8032

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EXAMINER	
SCHEINER, LAURIE A	
ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 03/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/816,531	Morimoto et al.
Examiner	**Art Unit**
Laurie Scheiner	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 27, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-19* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☒ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Claims 1-19 are pending in this application.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the city and state or foreign country of residence of each inventor.

Also, it does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen,* 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim,* 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). Claims 1-19 are drawn toward an attenuated recombinant rabies vaccine wherein a non-neuroinvasive recombinant rabies virus glycoprotein structural gene is replaced with a heterologous gene encoding a neuroinvasive glycoprotein. Additional limitations are provided concerning whether or not a pro-apoptotic gene is inserted, whether apoptosis is accelerated, or acceleration of apoptosis enhances an immune response against the virus. Claims 1-19 are drawn toward a

product consisting of a recombinant rabies virus containing any heterologous neuroinvasive rabies glycoprotein (replacement) gene or replacement codon resulting in a change of any amino acid at any position. The written description requirement under Section 112, first paragraph, sets forth that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have concluded that the specification must demonstrate that the inventor(s) had possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *In re Wilder, et al.,* 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Werthheim, et al.,* 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Driscoll,* 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter v. Hiraga,* 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California v. Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). *In re Bell,* 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993).

The significance of conception and reduction to practice was further addressed by the court in *Fiers v. Sugano* where it was emphasized that "[c]onception is a question of law, reviewed *de novo* on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated; thus, regardless of complexity or simplicity of method of isolation employed, conception of DNA sequence, like conception of any chemical substance, requires definition of that substance other than by its functional utility." Thus, the courts have emphasized that the inventor must clearly

and unambiguously identify the salient characteristics and properties of any given claimed nucleotide sequence. It is not sufficient to provide a vague reference to the biological activity of any given nucleotide sequence or merely a generic method of obtaining it.

Applicants' disclosure fails to provide adequate written support for the invention as **broadly** claimed. That is, applicants' claims encompass replacement regions encoding any rabies neuroinvasive glycoprotein or portions thereof. However, the disclosure merely provides discussion of CVS-N2c as the heterologous insert; or replacement of arginine at position 333 with glutamine. As such, limiting the scope of the claims commensurate with that which has been described in the specification would be acceptable. Again, the disclosure fails to provide an adequate written description for subject matter encompassing other gene variants or portions thereof which would function similarly with respect to proper expression, immunogenicity, etc.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. As set forth above, claims 1-19 are drawn toward a product consisting of a recombinant rabies virus containing a any heterologous neuroinvasive rabies glycoprotein (replacement) gene or replacement codon resulting in a change of any amino acid at any position. Moreover, due to the recitation of "vaccine" it is assumed that the recombinant may be admixed with a pharmaceutically acceptable carrier. It is asserted that the claims as reasonably interpreted could encompass virtually any nucleotide sequence encoding virtually any G protein antigen or epitope, however, the breadth is not adequately supported by the disclosure since relatively few examples have been elucidated. Applicants are reminded of the legal considerations governing enablement determinations pertaining to undue experimentation as disclosed in *In re Wands,* 8

U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer,* 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to meet the legal requirements dictating that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher,* 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck,* 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). *In re Angstadt,* 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). The court stated in *In re Vaeck* that "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility. Where, as here, a claimed genus represents a diverse and relatively poorly understood group of encoded antigens, the required level of disclosure will be greater than, for example, the disclosure of an invention involving a "predictable" factor such as a mechanical or electrical element."

In summation, the disclosure fails to provide sufficient guidance pertaining to the molecular determinants modulating the attenuated protective activity of any given recombinant rabies virus containing sequence encoding any given neuroinvasive (somewhat relative term) G protein, the disclosure fails to provide sufficient guidance pertaining to those variants or derivatives that can reasonably be expected to have and retain stable protective activity.

Furthermore, the prior art fails to provide sufficient guidance pertaining to the structural requirements of analogous elements. Thus, the skilled artisan could not possibly predict the nucleotide sequence of various functional equivalents. Accordingly, when all the aforementioned factors are considered together, it would clearly require undue experimentation to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-19 are vague and indefinite in their recitation of "glycoprotein gene of a neuroinvasive rabies virus". The genes have not been defined by structure and the extent of subject matter to which the exclusionary right granted by patent is intended to apply can not be determined since the rabies G proteins consist of a wide array of variants. Moreover, it appears that "neuroinvasive" is a relative term depending on host species. Again it is not possible for one to determine from the claims what they comprehend since they require explanations extraneous to both the specification and the claims. Which G protein gene portions are intended? Applicants are reminded that the claims must be so definite as to allow their comparison with the available art and must also make it possible for the public to determine from the claims what they encompass and/or exclude. The "change in amino acid" of claim 6 has not been defined by structure. Definite claim language is important for at least two reasons. First, a member of the public must be able to understand what is encompassed by the claims for potential infringement purposes. Second, the claims must be drafted in a definite manner in order that the subject

matter may be reasonably compared with the prior art. It has been indicated in several prior decisions that claims may be too indefinite to be examined with respect to the prior art. It is asserted that determining anticipation in the present case would involve the type of "*speculation*" proscribed by the decision in *In re Steele*. That is, in *In re Steele*, 305 F.2d 859, 134 USPQ 292 (CCPA 1962), the court pointed out that before the claimed subject matter could properly be compared to the prior art, it was essential to know what in fact the claims did cover.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-19 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Morimoto et al. (JOURNAL OF NEUROBIOLOGY (October 2000) Vol. 6, No. 5, pp.373-381).

Morimoto et al. clearly anticipate that which is instantly claimed. Morimoto et al. clearly teach modification of the G protein by exchanging arginine at position 333 for glutamine and modifications of the cytoplasmic domain resulting in live oral rabies vaccines having the ability to confer protective immunity. It is noted that the rejection may be addressed by the filing of a Katz or disclaiming declaration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Scheiner, whose telephone number is (703) 308-1122. Due to a flexible work schedule, the examiner's hours typically vary each day. However, the examiner can normally be reached Monday thru Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242, (703) 305-3014, (703) 872-9306 or (703) 872-9307. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 746-5226.

Laurie Scheiner/LAS
March 22, 2002

LAURIE SCHEINER
PRIMARY EXAMINER